Online Supplement

Supplemental Methods

Setting

Uganda is one of the world's 30 countries with the highest burdens of TB and HIV [1]. The national TB prevalence is 253/100,000 and 46% of those with prevalent TB have not been diagnosed or reported to public health authorities [2].

Exclusion criteria

CHWs excluded index patients who declined or were unable to consent; were homeless or lived alone; lacked access to a mobile phone; or did not speak English or Luganda. In addition, those who lived outside Kampala or had multi-drug-resistant(MDR) TB were referred to outside treatment units and excluded from further study. CHWs excluded contacts who declined screening or did not provide consent; were already receiving TB treatment; lacked access to a mobile phone; were unwilling to receive personal health information via SMS; did not meet the definition of a household contact (spent ≥3 days or nights in last 30 days sleeping under same roof as index patient) or did not speak English or Luganda.

Procedures

The CommCare survey application was deployed on password-protected Android tablets. Data were automatically uploaded to a cloud-based server (CommCareHQ) via 3G wireless connections as soon as accessible. To exclude duplicate enrollment and verify follow-up visits, CHWs collected encrypted biometric data (thumb and index finger on each hand) for

participants aged ≥5 years using multi-spectral, digital fingerprinting scanners (Lumidigm M301, HID Global, Austin, TX, USA) and fingerprint-matching software (Biometrac, Louisville, KY, USA) deployed within the survey application.

HIV status within the decision-support algorithm was determined by self-report in the standard of care arm and through self-report supplemented by the results of home-based HIV testing for consenting individuals ≥15 years of age in the intervention arm. HIV testing was carried out by CHWs who collected capillary blood by finger prick after consent and performed rapid ELISA assays on-site following the Uganda national serial-testing algorithm.[3]

Five clinics had GeneXpert machines on site and two clinics referred smear-negative samples to the other clinics for testing. CHWs adjusted the number of samples requested depending on the availability and functionality of GeneXpert for testing. CHWs collected one sample if GeneXpert machines and cartridges were available on site and operational at the time of evaluation, or, if not, they collected two samples for smear microscopy.

Those not diagnosed with TB were scheduled to receive automated SMS inquiring about TB symptoms at six monthly intervals for two years.

Sample size

We initially projected a sample size of 544 patients, but after the first interim analysis, we updated this target to 774. We carried out quarterly interim analyses of sample size only. These

analyses were blinded to allocation arm and assessed the numbers of contacts enrolled, the average number of contacts per household, the aggregated proportion completing evaluation across the two arms, the intraclass correlation(ICC), and the design effect. Our sample size calculations assumed 50% of household contacts would be identified as requiring additional TB evaluation, a within-household ICC of 0.48, and an average of 2.5 contacts per household, giving a design effect of 1.7. Blinded interim assessments of this kind have been shown to have no material effect on the type-I error rate [4].

Randomization

The study statistician (E.V.) generated the allocation sequences in variable, balanced blocks of four or six assignments using the *ralloc* command in Stata Version 13.1. Sequences were stratified by index patient age (adults ≥15 years, older children aged 5-14 years, young children aged ≤5 years), HIV status, and enrolling CHW, the latter in order to balance community-level characteristics and to enable offline allocation if necessary. A Dimagi programmer loaded allocation sequences to a hidden, password-protected location on each CHW's tablet before the trial was launched. Each allocation was assigned when CHWs submitted enrollment information for the index patient to the survey software and revealed after contact enrollment procedures had been completed.

Supplemental Results

There were 14 CHWs in total (mode 2 per site, range 1-3).

We stopped the trial upon exceeding the target enrollment at the 12-month interim analysis. We encountered 1193 household contacts of 1228 (97%) household contacts identified by index patients.

The median age of index patients was 29 years (interquartile range, IQR, 23-37) for both study arms (p=0.99). Index patients were predominantly male in both the intervention (n=110, 58%) and standard-of-care(n=101, 55%) arms(p=0.64). Sixty-four (34%) patients in the intervention arm and 63 (35%) index patients in the standard-of-care arm were PLWH (p=0.98). The median number of contacts reported by index patients was 3 (range 1-12) in both the intervention and the standard-of-care arms (p=0.78).

Among the 56/91 (41%) intervention-arm contacts who were possible TB patients based on symptoms and eligible for sputum collection but yet did not produce sputum and were referred to clinic; 10/56 (18%) of these completed evaluation at clinic within 60 days of the initial home visit.

Longitudinal SMS

Among 461 intervention contacts without confirmed prevalent TB, longitudinal follow-up messages inquiring about TB symptoms were initiated for 320 contacts at six months and 132 contacts at 12 months. No longitudinal SMS were documented in the SMS application for 141 contacts. There were no clinical or demographic differences between those who did and did not receive longitudinal SMS, although non-recipients were clustered in two time periods.

Supplemental References

1. World Health Organization. Global tuberculosis control: WHO Report 2016. Geneva: World Health Organization; 2016.

2. Uganda Ministry of Health. The Uganda National Tuberculosis Prevalence Survey 2014-2015 Report. Kampala: Ministry of Health; 2017.

3. Uganda Ministry of Health. National HIV Testing Services Policy and Implementation Guidelines Uganda. 4th ed. Kampala: Ministry of Health; 2016.

4. Gould AL. Interim analyses for monitoring clinical trials that do not materially affect the type I error rate. Stat Med. 1992;11(1):55-66. Epub 1992/01/15. PubMed PMID: 1557576.

Supplemental Tables and Figures

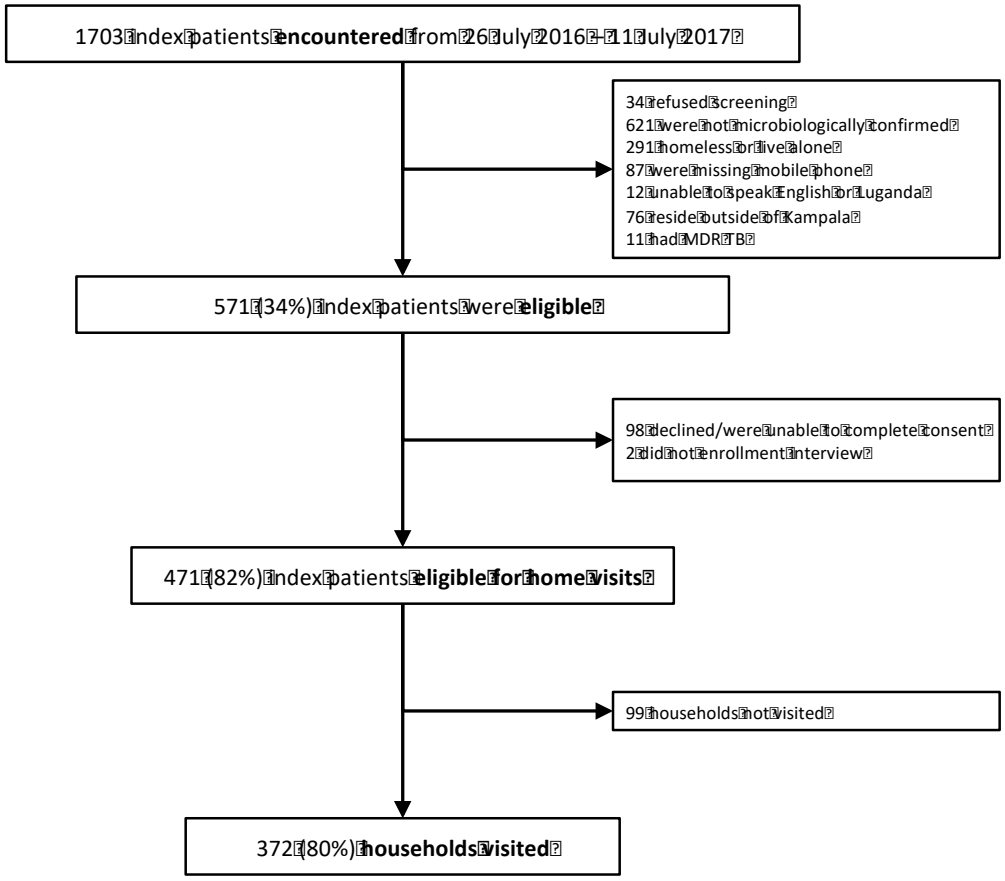

Figure S1. Flow diagram showing enrollment of index patients.
Abbreviations: MDR TB, multi-drug resistant tuberculosis;

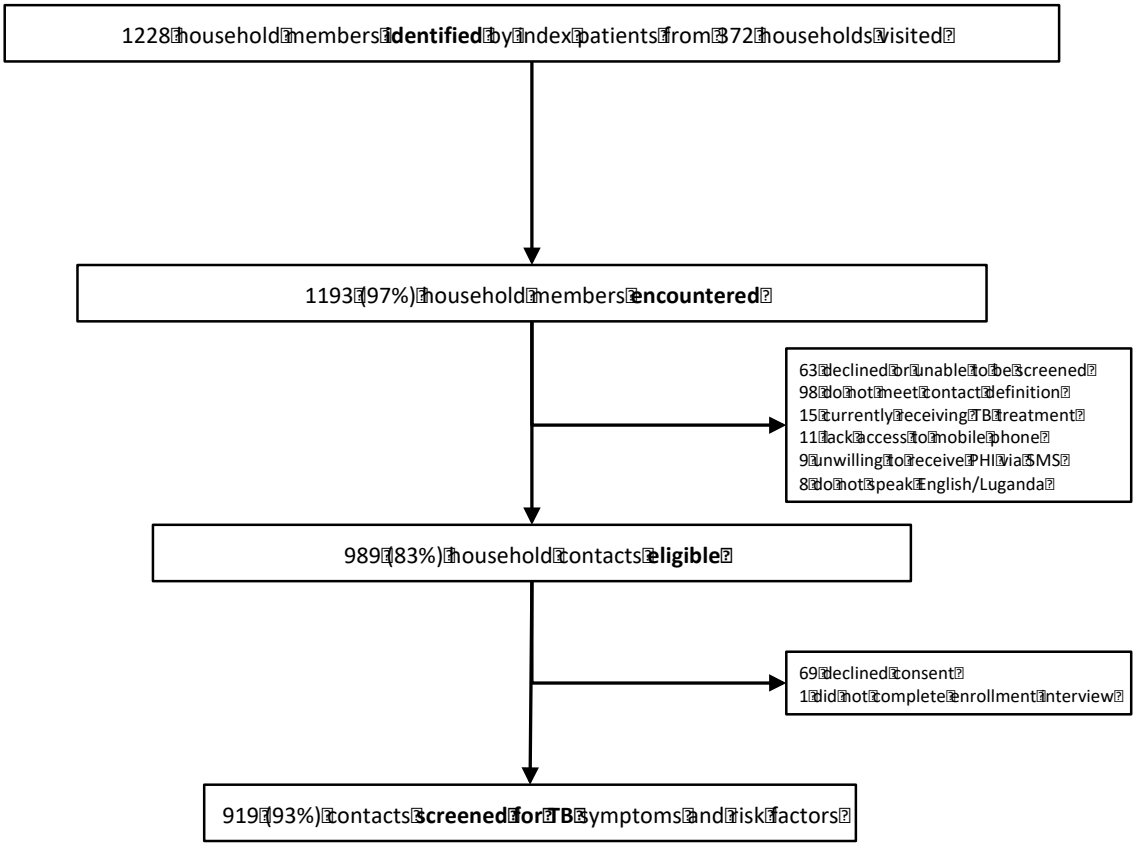

Figure S2. Flow diagram showing enrollment of household contacts.
Abbreviations: TB, tuberculosis; **PHI**, personal health information; **SMS**, short message service messages

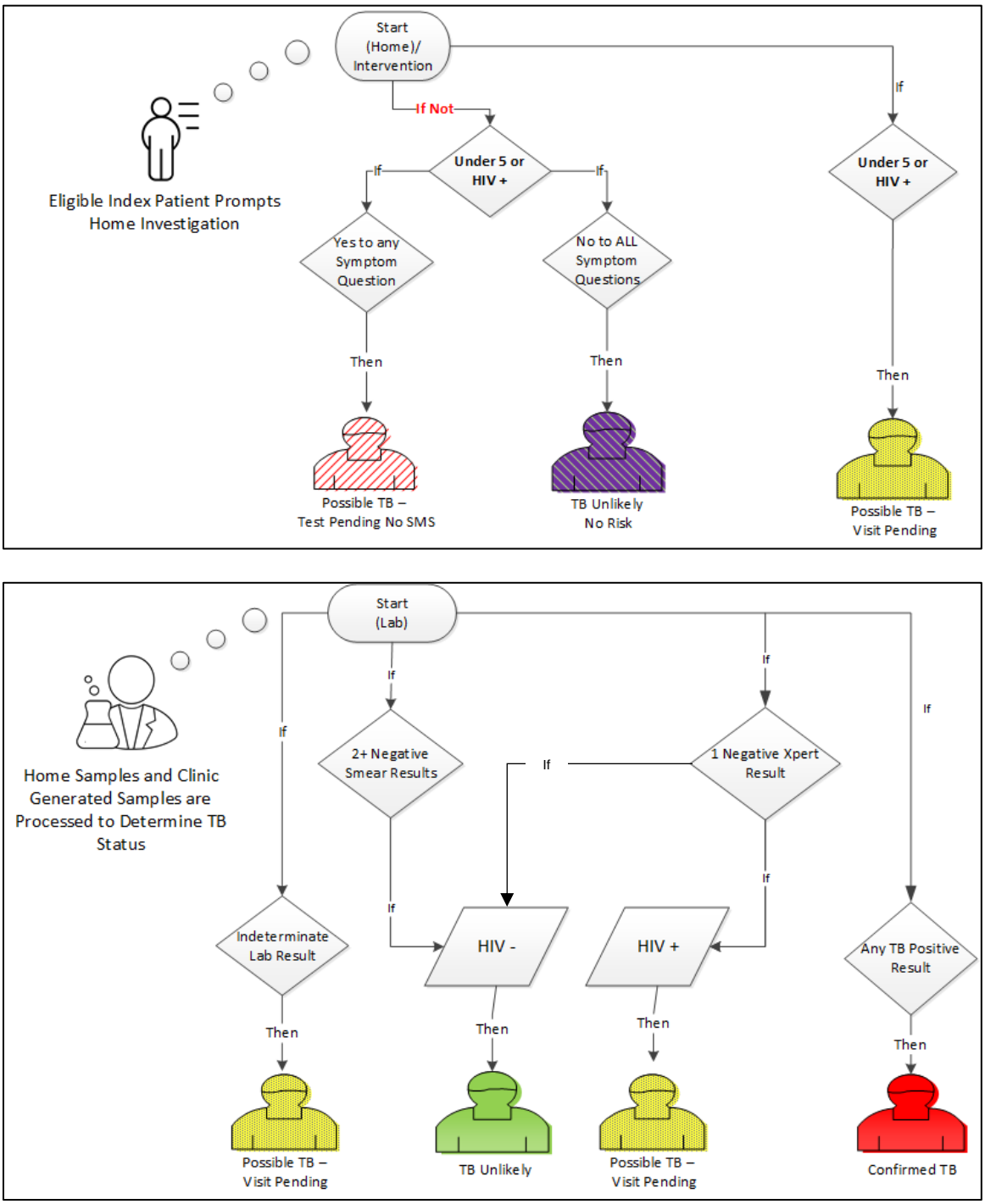

Figure S3. **Automated decision-support algorithm for TB evaluation.** Individual data collected by CHWs and entered into the survey application was used to assign contacts into pre-specified categories for delivery of SMS content. The upper box shows the TB screening process for household contacts; the lower box shows the laboratory testing process for sputum collected from eligible contacts. Symptom questions were based on WHO Contact Investigation guidelines: cough ≥2 weeks, fever, night sweats, or weight loss ≥3 kg, with sputum requested from anyone ≥ 5 years of age with TB symptoms or HIV.

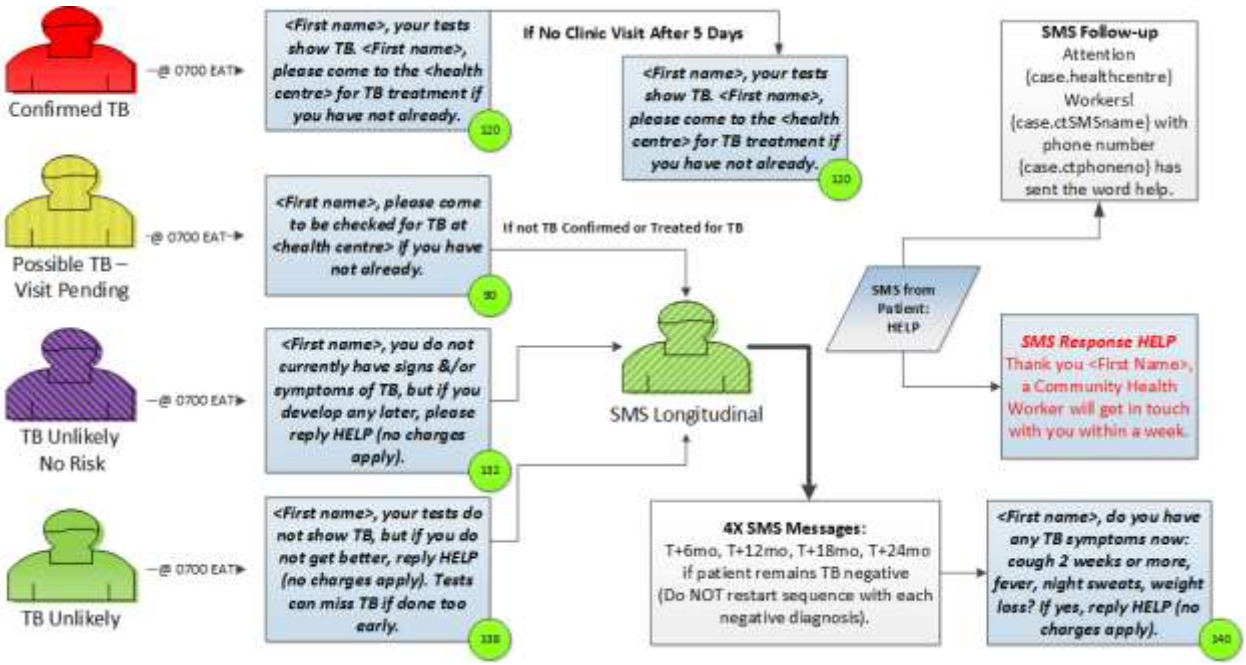

Figure S4. SMS content and delivery algorithm displaying the five states of contact evaluation(four baseline and one longitudinal) at the left side of the figure. Message content was refined through focus groups with household contacts, as previously described [26]. Green circles show the character count of each SMS. The algorithm for delivery and response to reply SMS sent by contacts is shown at the upper right of the figure. All reply SMS sent from contact phones that included the word “Help” triggered an alert SMS to the phones of community health workers attached to the health center responsible for that contact household. The alert SMS included the name and phone number of that contact. An SMS confirming receipt of the reply message and promising a response from a community health worker was also returned to the contact’s phone.